Amino Acids and Peptides

Amino acids

- Amino acids share a common structure
- The different chemical properties of amino acids are the result of different properties of their R groups, which are the basis for categorizing amino acids as nonpolar, aromatic, polar, positively charged, or negatively charged
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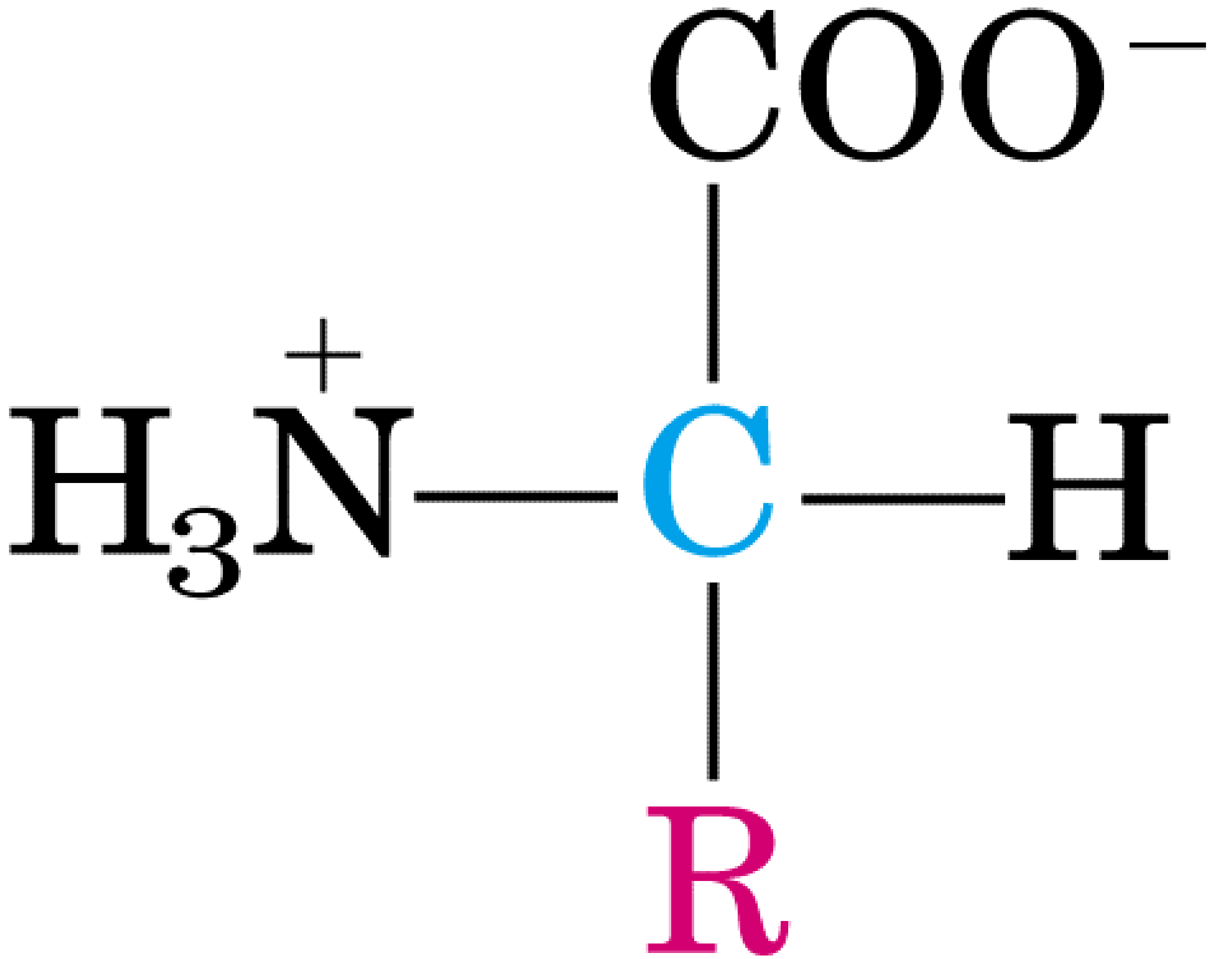
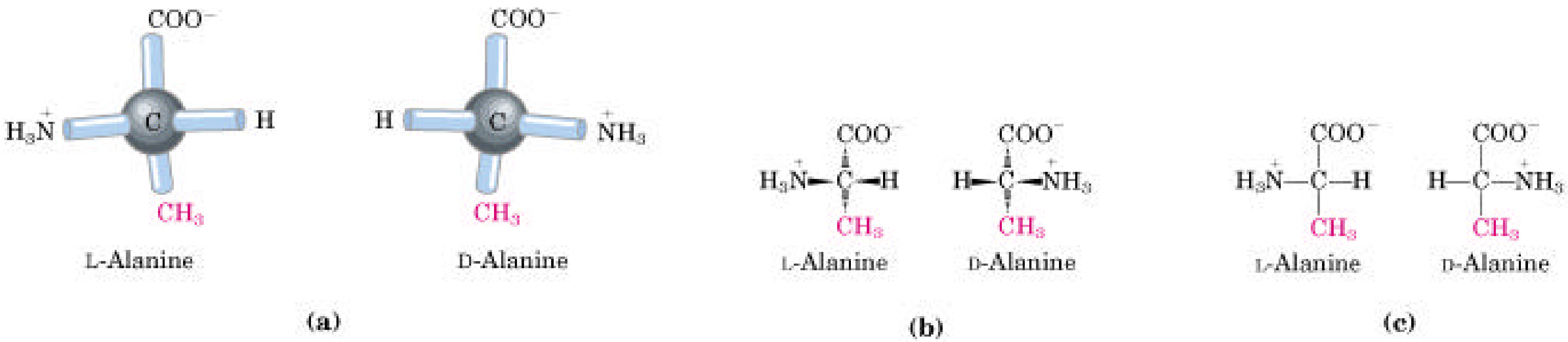
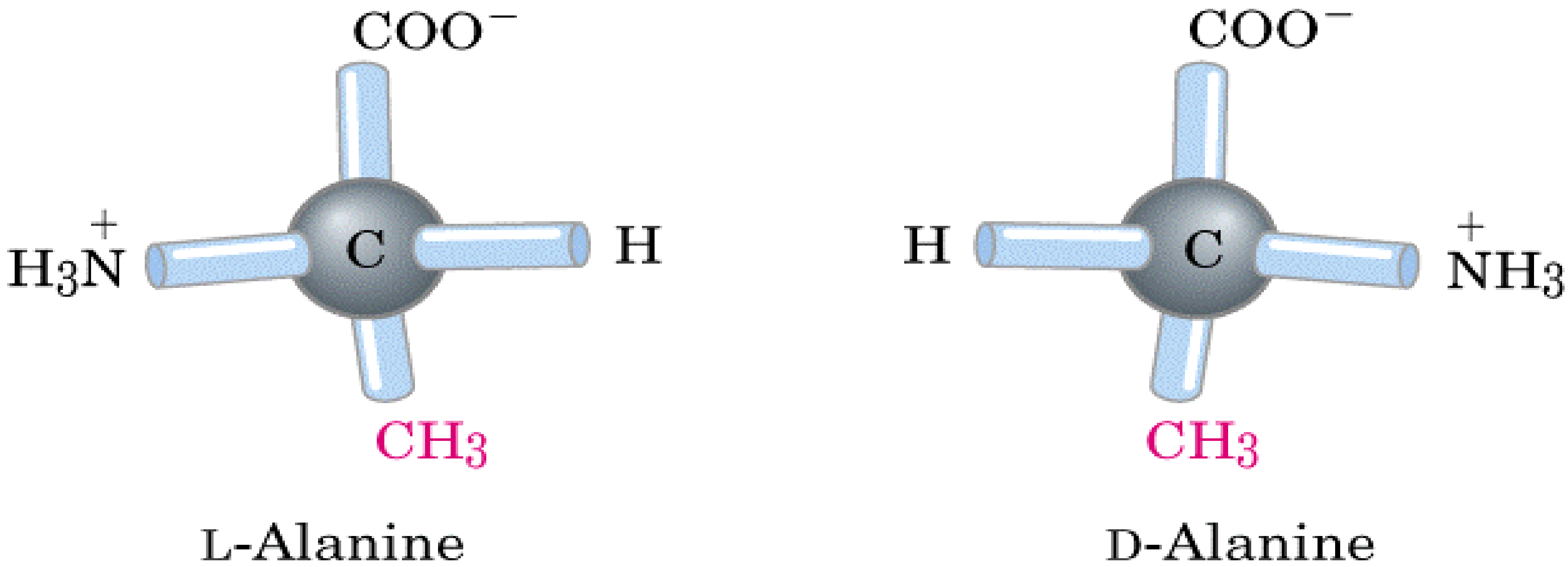


General Structure of an Amino Acid: The R group or side chain attached to the *a* carbon is different in each amino acid.



Different conventions for showing the configurations in space of stereoisomers: In perspective formulas (b), the wedge-shaped bonds project out of the plane of the paper, the dashed bonds behind it. In projection formulas, (c) the horizontal bonds are presumed to project out of the plane of the paper, the vertical bonds behind it.



Stereoisomerism in *α* amino acids: the *α* C is bonded to four different groups and is thus a chiral center. The tetrahedral arrangement of bonding orbitals around the *α* C means the four groups can occupy two different spatial arrangements that are non-superimposible images of each other. These two forms represent a class of stereoisomers called enantiomers, and are optically active.

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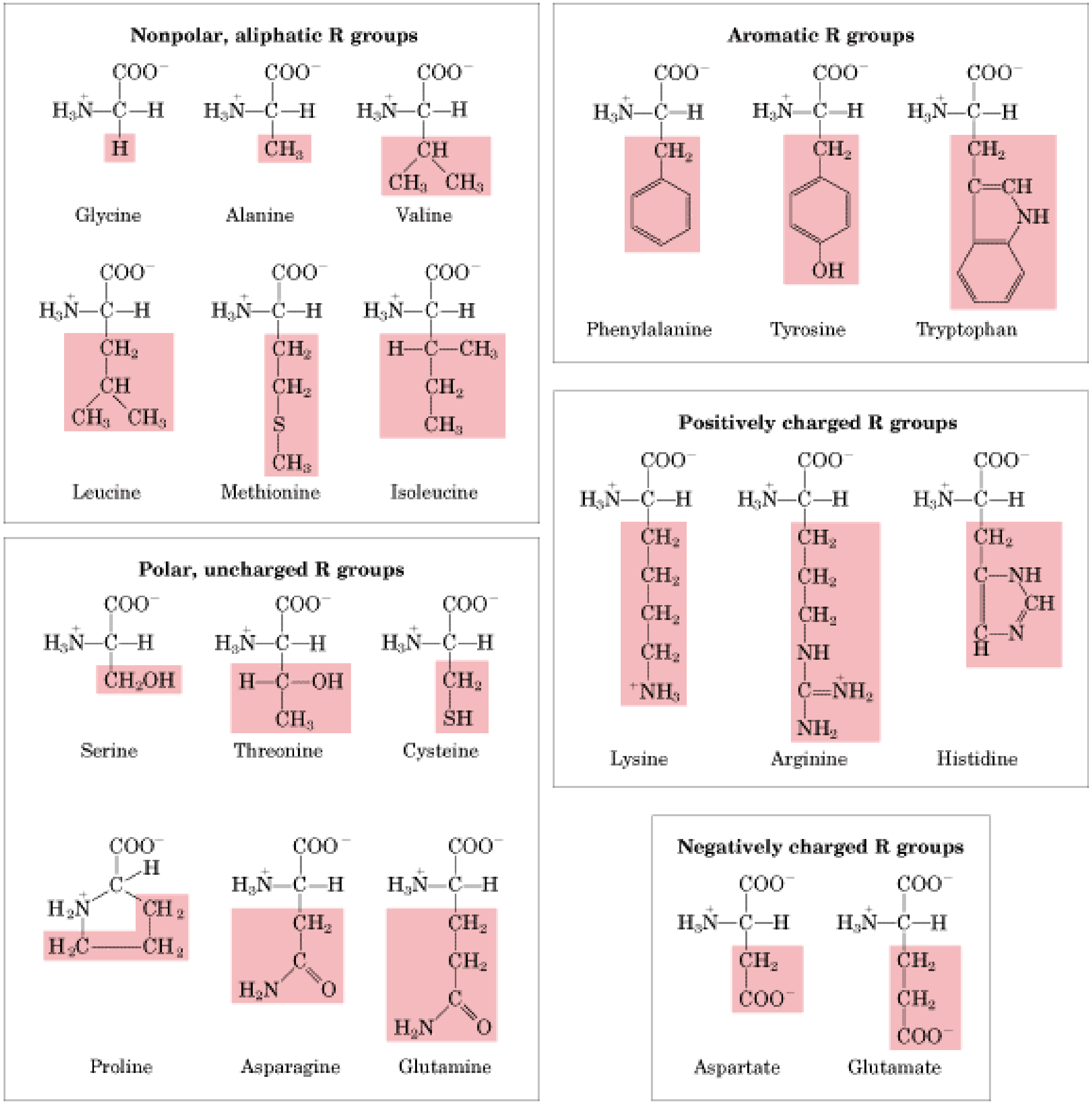
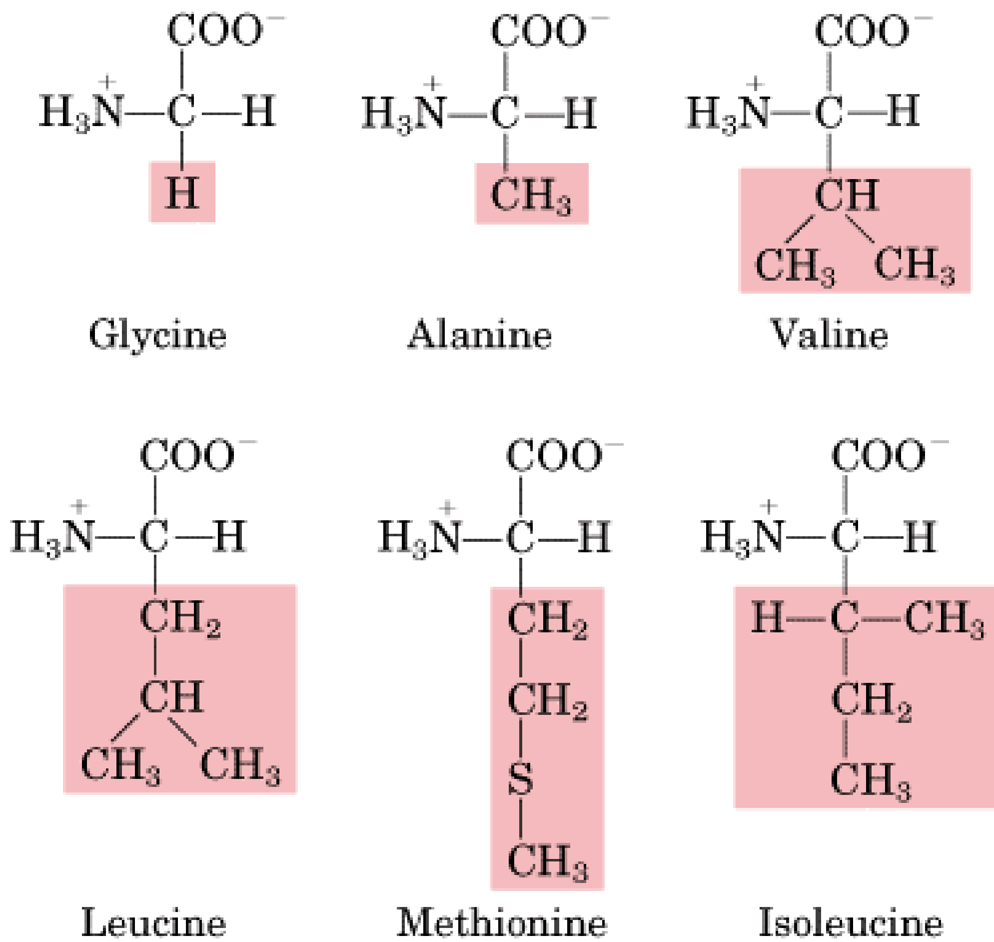
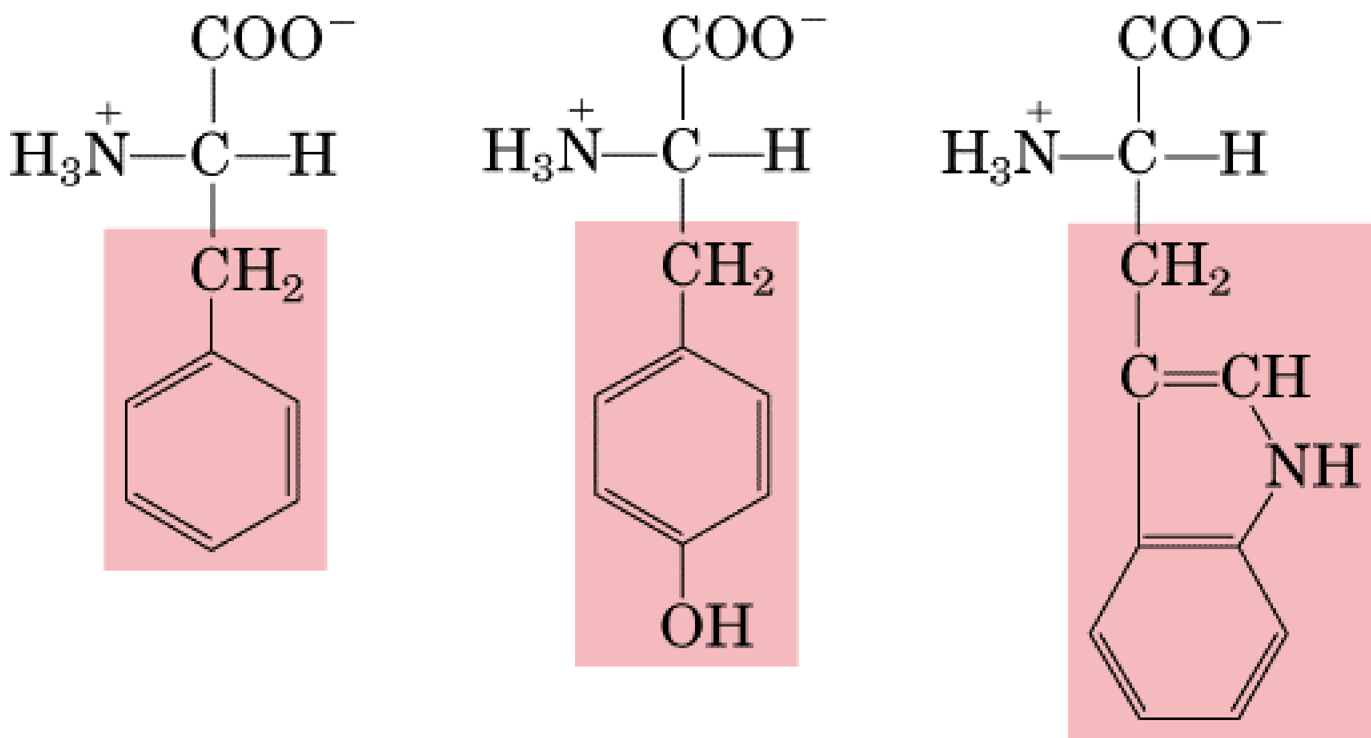

Nonpolar, aliphatic R groups
Glycine
Alanine
Valine
Leucine
Methionine
Isoleucine
Aromatic R groups
Phenylalanine
Tyrosine
Tryptophan
Polar, uncharged R groups
Serine
Threonine
Cysteine
Proline
Asparagine
Glutamine
Positively charged R groups
Lysine
Arginine
Histidine
Negatively charged R groups
Aspartate
Glutamate

Nonpolar, aliphatic R groups

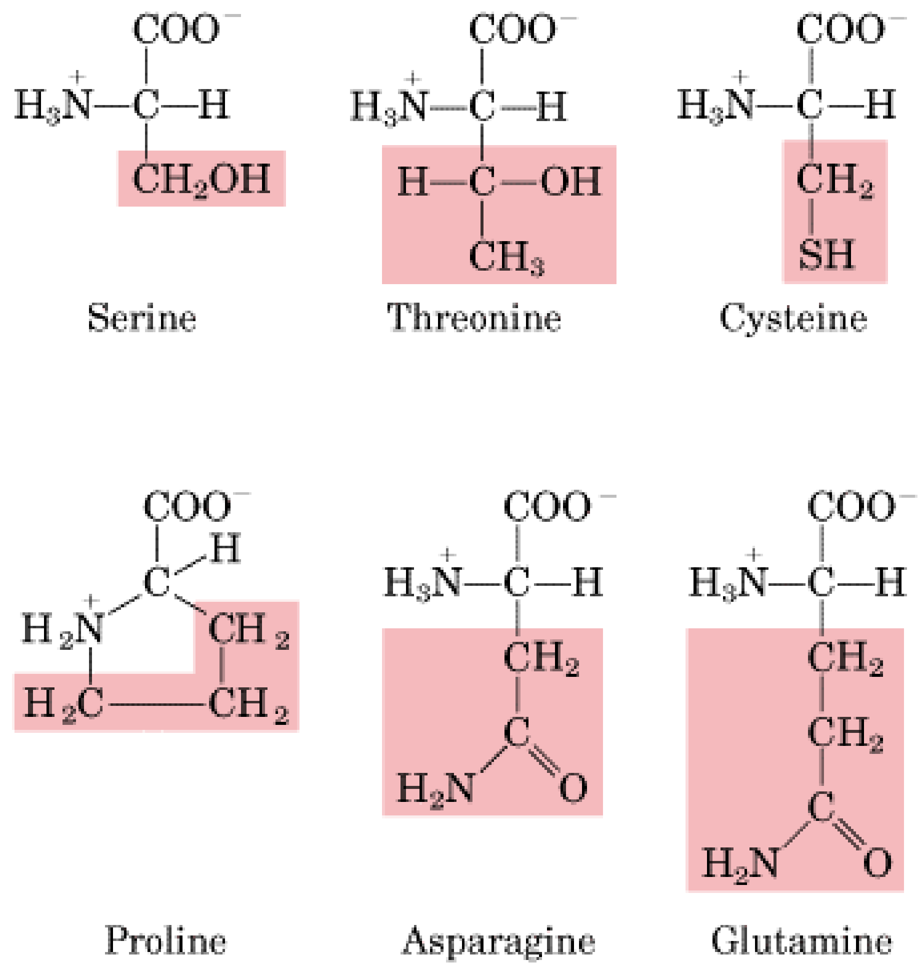


Aromatic R groups

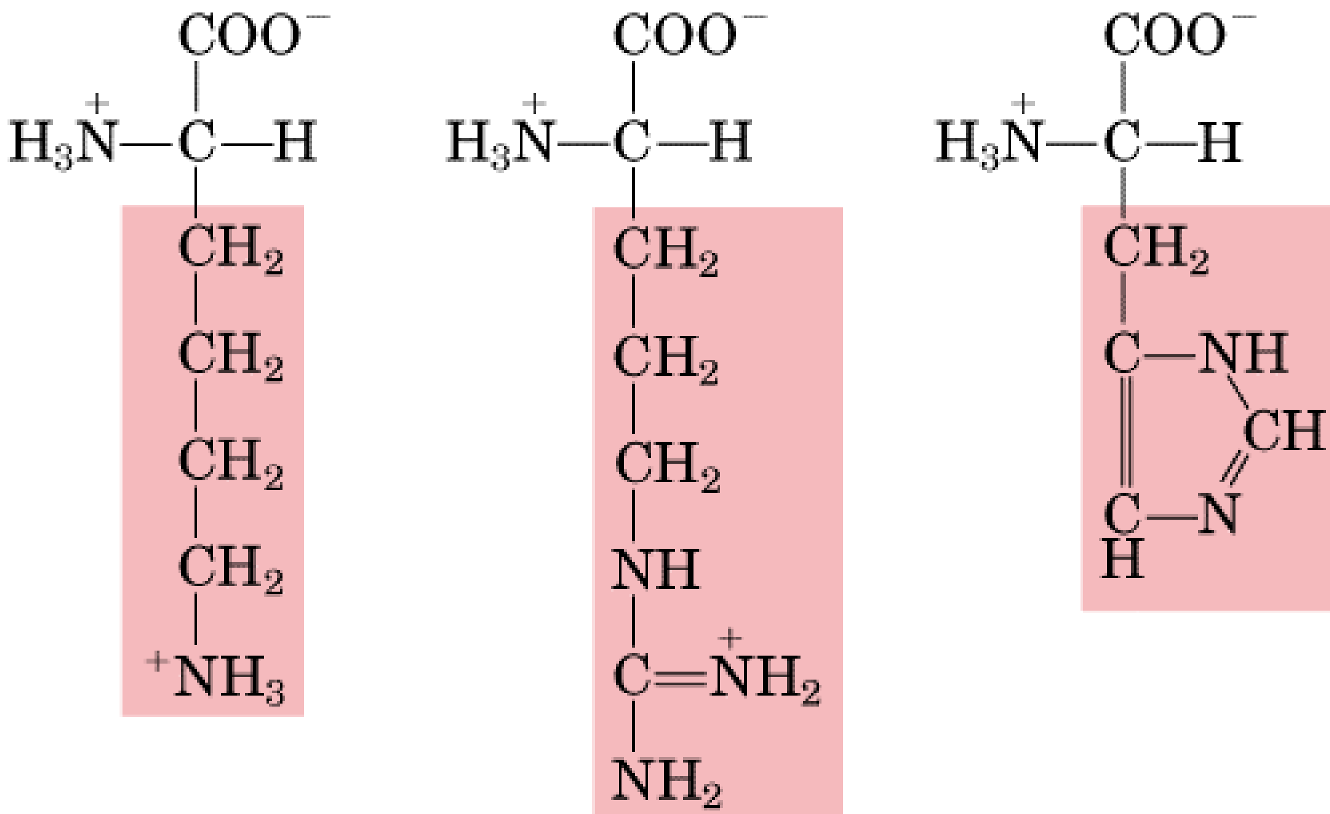


Phenylalanine Tyrosine Tryptophan

Polar, uncharged R groups

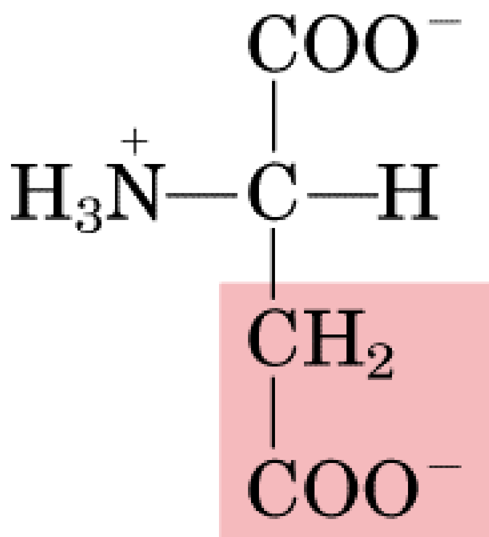


Positively charged R groups

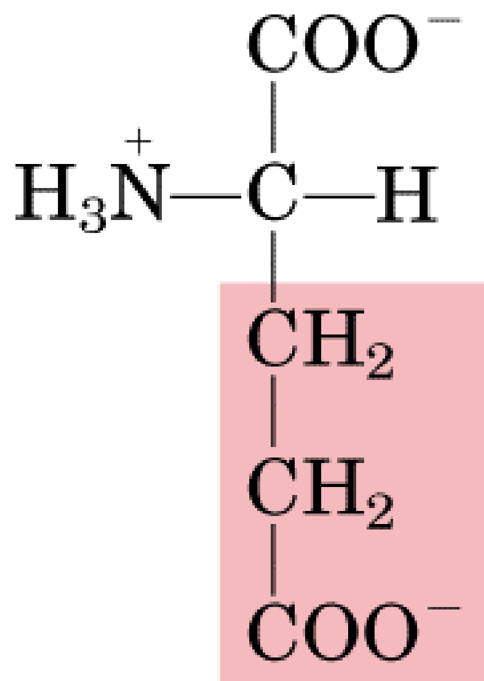


Lysine Arginine Histidine

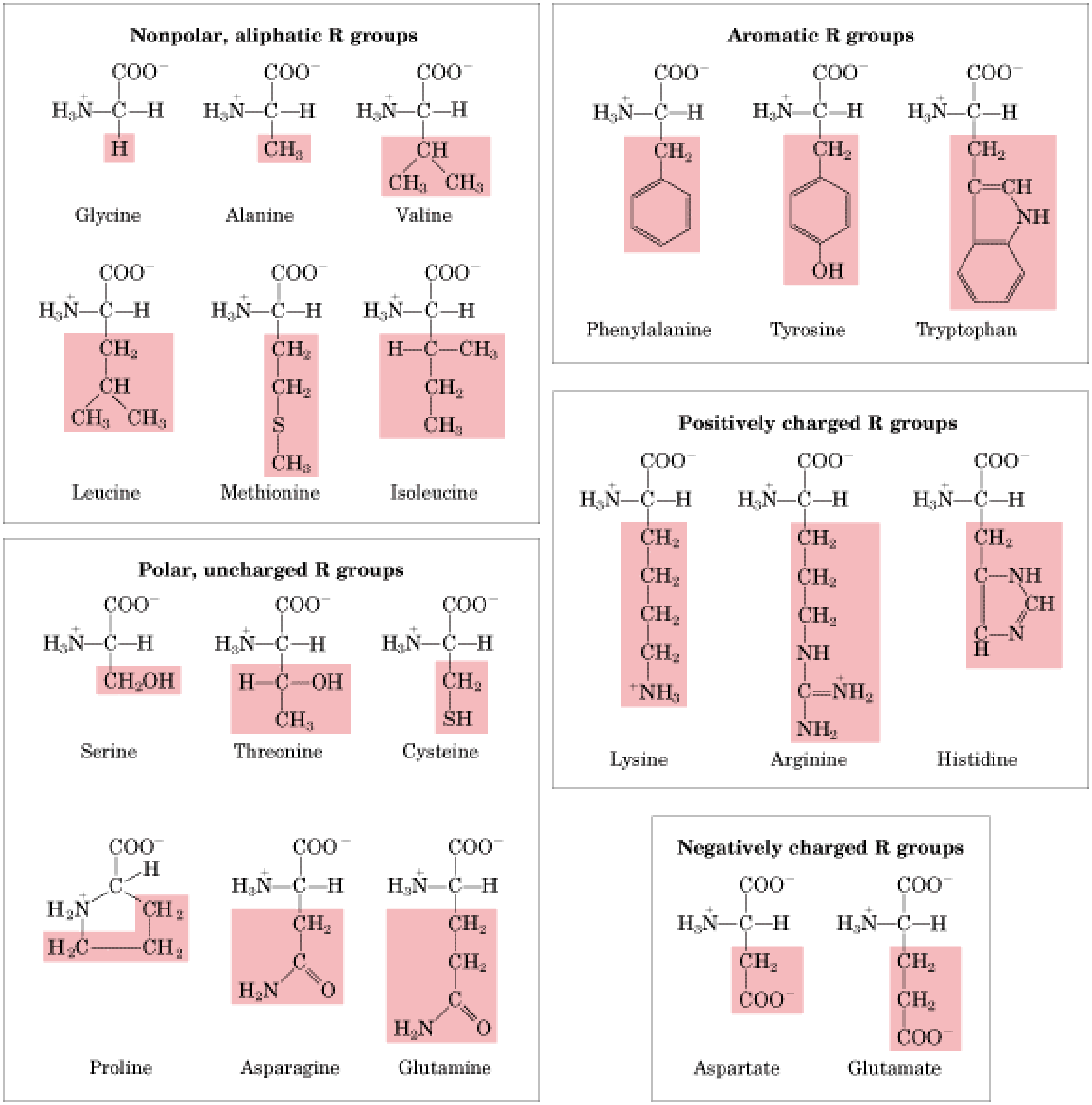
Negatively charged R groups



Aspartate



Glutamate


Nonpolar, aliphatic R groups
Glycine
Alanine
Valine
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Tryptophan
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Serine
Threonine
Cysteine
Proline
Asparagine
Glutamine
Positively charged R groups
Lysine
Arginine
Histidine
Negatively charged R groups
Aspartate
Glutamate

table 5–1

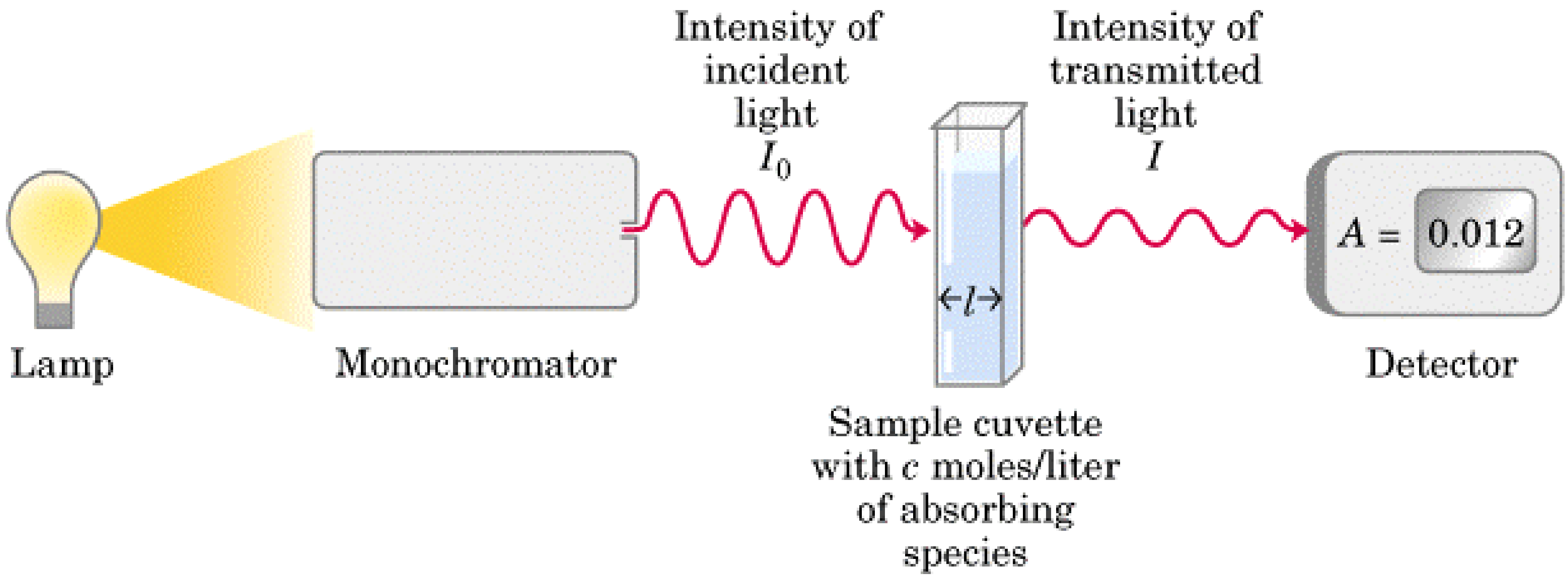
Properties and Conventions Associated with the Standard Amino Acids

Amino acid	Abbreviated names		M_r	pK_a values: pK_1 (—COOH)	pK_2 (—NH_3^+)	pK_R (R group)	pI	Hydropathy index*	Occurrence in proteins (%)[†]
Nonpolar, aliphatic R groups									
Glycine	Gly	G	75	2.34	9.60		5.97	−0.4	7.2
Alanine	Ala	A	89	2.34	9.69		6.01	1.8	7.8
Valine	Val	V	117	2.32	9.62		5.97	4.2	6.6
Leucine	Leu	L	131	2.36	9.60		5.98	3.8	9.1
Isoleucine	Ile	I	131	2.36	9.68		6.02	4.5	5.3
Methionine	Met	M	149	2.28	9.21		5.74	1.9	2.3
Aromatic R groups									
Phenylalanine	Phe	F	165	1.83	9.13		5.48	2.8	3.9
Tyrosine	Tyr	Y	181	2.20	9.11	10.07	5.66	−1.3	3.2
Tryptophan	Trp	W	204	2.38	9.39		5.89	−0.9	1.4
Polar, uncharged R groups									
Serine	Ser	S	105	2.21	9.15		5.68	−0.8	6.8
Proline	Pro	P	115	1.99	10.96		6.48	1.6	5.2
Threonine	Thr	T	119	2.11	9.62		5.87	−0.7	5.9
Cysteine	Cys	C	121	1.96	10.28	8.18	5.07	2.5	1.9
Asparagine	Asn	N	132	2.02	8.80		5.41	−3.5	4.3
Glutamine	Gln	Q	146	2.17	9.13		5.65	−3.5	4.2
Positively charged R groups									
Lysine	Lys	K	146	2.18	8.95	10.53	9.74	−3.9	5.9
Histidine	His	H	155	1.82	9.17	6.00	7.59	−3.2	2.3
Arginine	Arg	R	174	2.17	9.04	12.48	10.76	−4.5	5.1
Negatively charged R groups									
Aspartate	Asp	D	133	1.88	9.60	3.65	2.77	−3.5	5.3
Glutamate	Glu	E	147	2.19	9.67	4.25	3.22	−3.5	6.3

*A scale combining hydrophobicity and hydrophilicity of R groups; it can be used to measure the tendency of an amino acid to seek an aqueous environment (− values) or a hydrophobic environment (+ values). See Chapter 12. From Kyte, J. & Doolittle, R.F. (1982) *J. Mol. Biol.* **157**, 105 – 132.

†Average occurrence in over 1150 proteins. From Doolittle, R.F. (1989) Redundancies in protein sequences. In *Prediction of Protein Structure and the Principles of Protein Conformation* (Fasman, G.D., ed) Plenum Press, NY, pp. 599–623.

Measurement of Amino Acids and Peptides

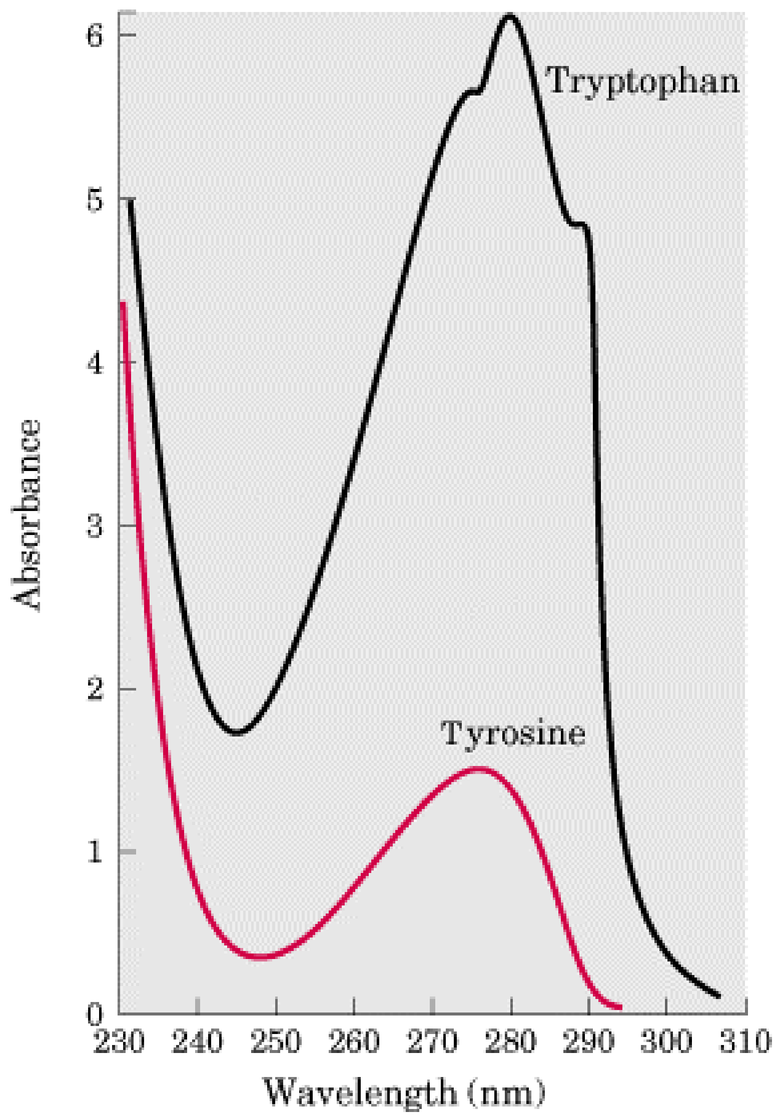


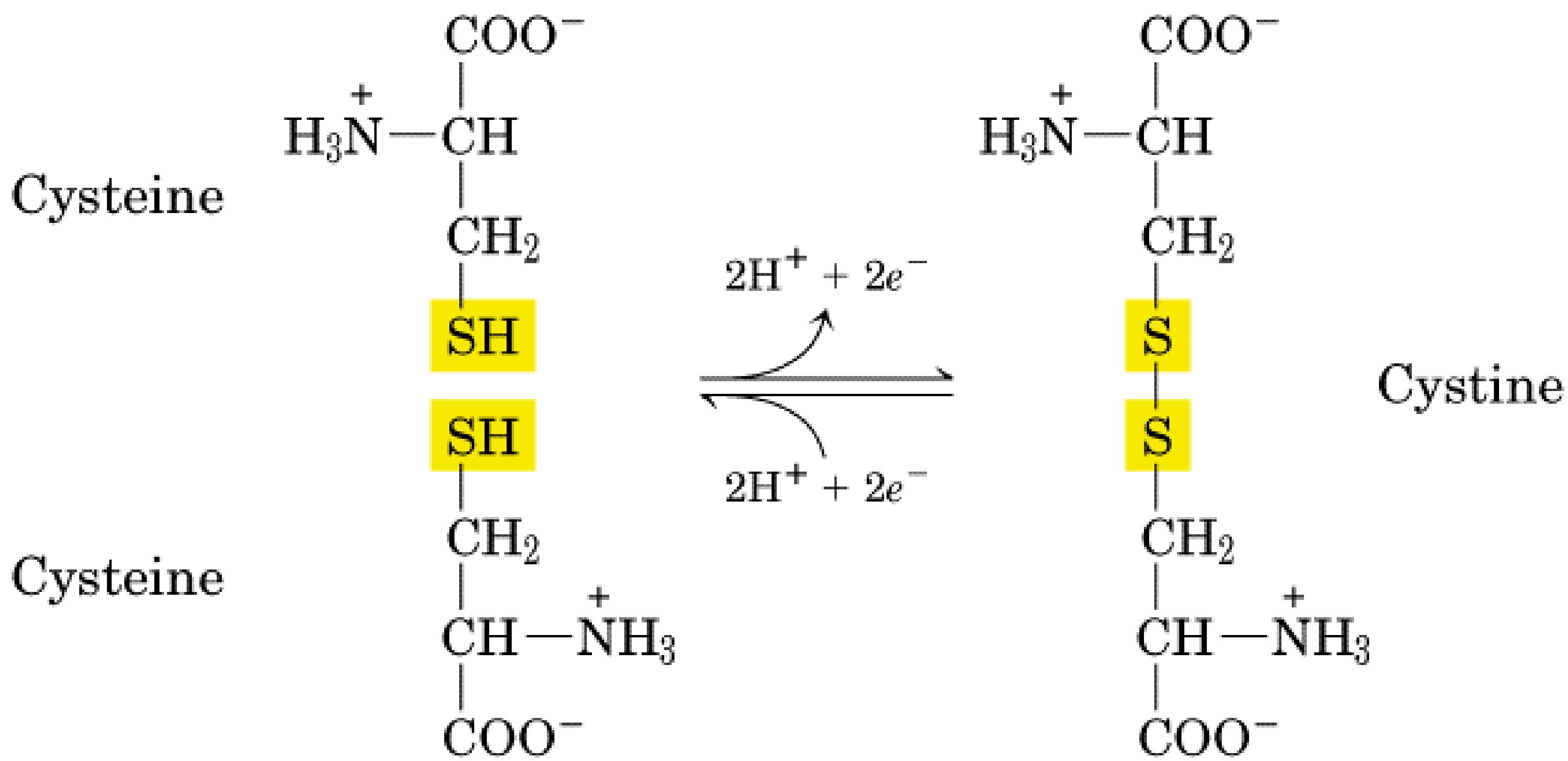
Absorption of Light by Molecules: The Lambert-Beer Law

The fraction of the incident light absorbed by a solution at a given wavelength is related to the thickness of the absorbing layer (path length) and the concentration of the absorbing species. *The absorbance is directly proportional to the concentration of the absorbing solute.*

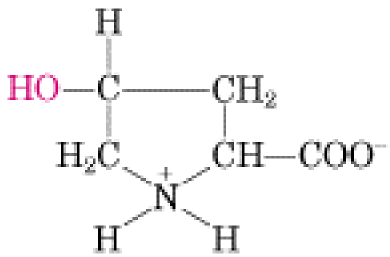
Absorbance of ultraviolet light by aromatic amino acids:

The light absorbance of tryptophan (W) is as much as fourfold higher than that of tyrosine (Y). The absorbance maxima for both W and Y occur near a wavelength of 280nm. Light absorbance by the third aromatic amino acid, phenylalanine (F, not shown), generally contributes little to the absorbance properties of proteins.

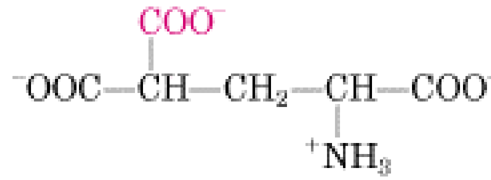




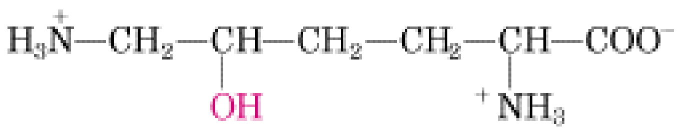
Reversible formation of a disulfide bond by the oxidation of two molecules of cysteine (C): Disulfide bonds between C residues stabilize the structures of many proteins. Note that, although C is a *polar* AA, the disulfide-linked residues (Cystine) are *strongly hydrophobic*.



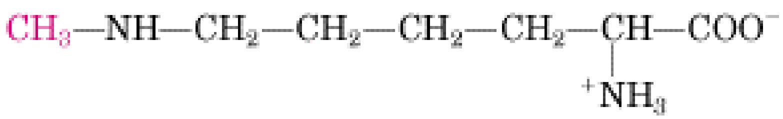
4-Hydroxyproline



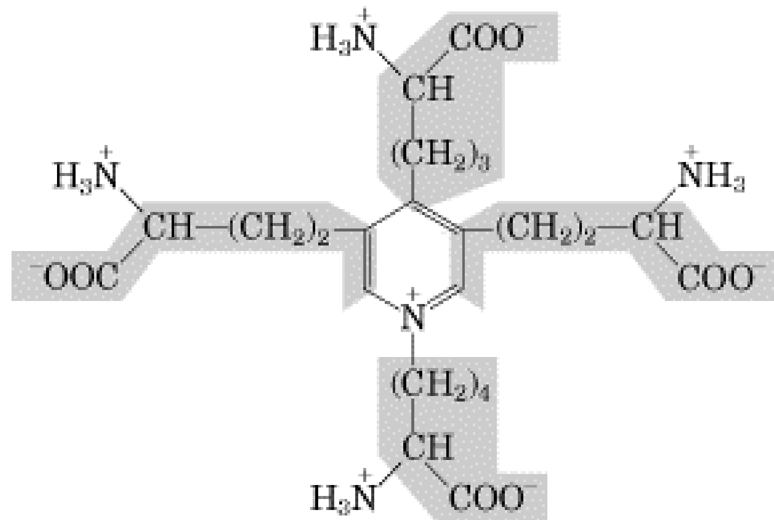
γ-Carboxyglutamate



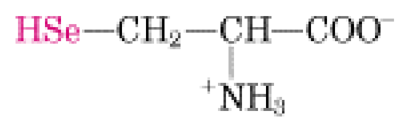
5-Hydroxylysine



6-*N*-Methyllysine

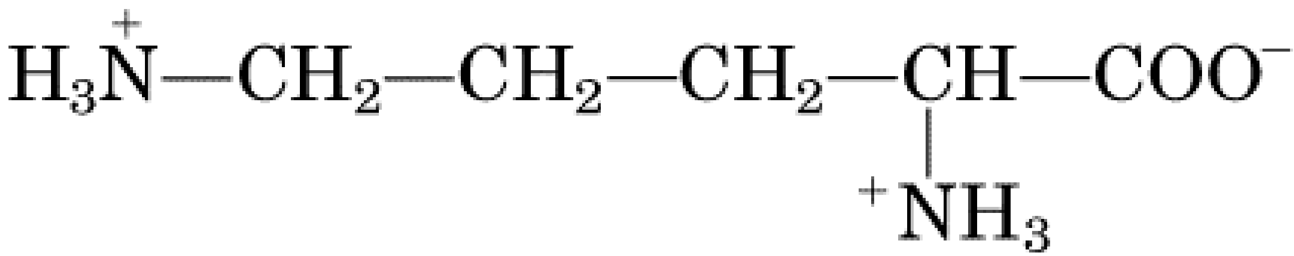


Desmosine

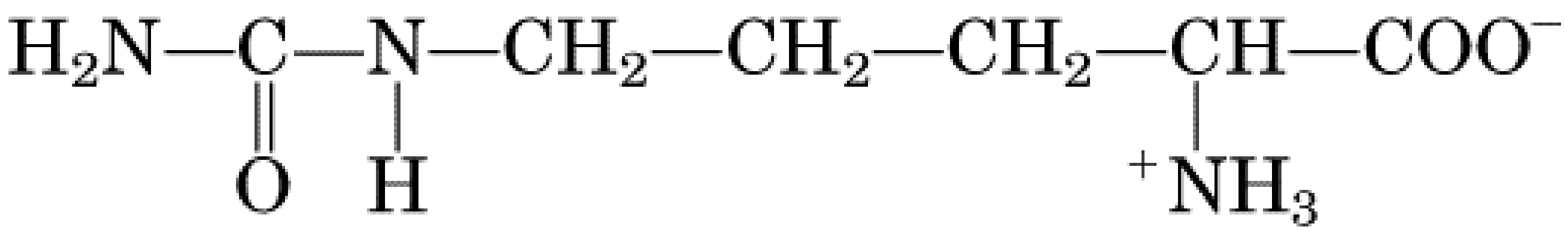


Selenocysteine

Nonstandard amino acids found in proteins: All are derived from standard amino acids. Extra functional groups added by modification reactions are shown in red. Desmosine is formed from four Lysine (K) residues.



Ornithine



Citrulline

Nonstandard amino acids: Ornithine and Citrulline, which are not found in proteins, are intermediates in the biosynthesis of arginine and in the urea cycle.

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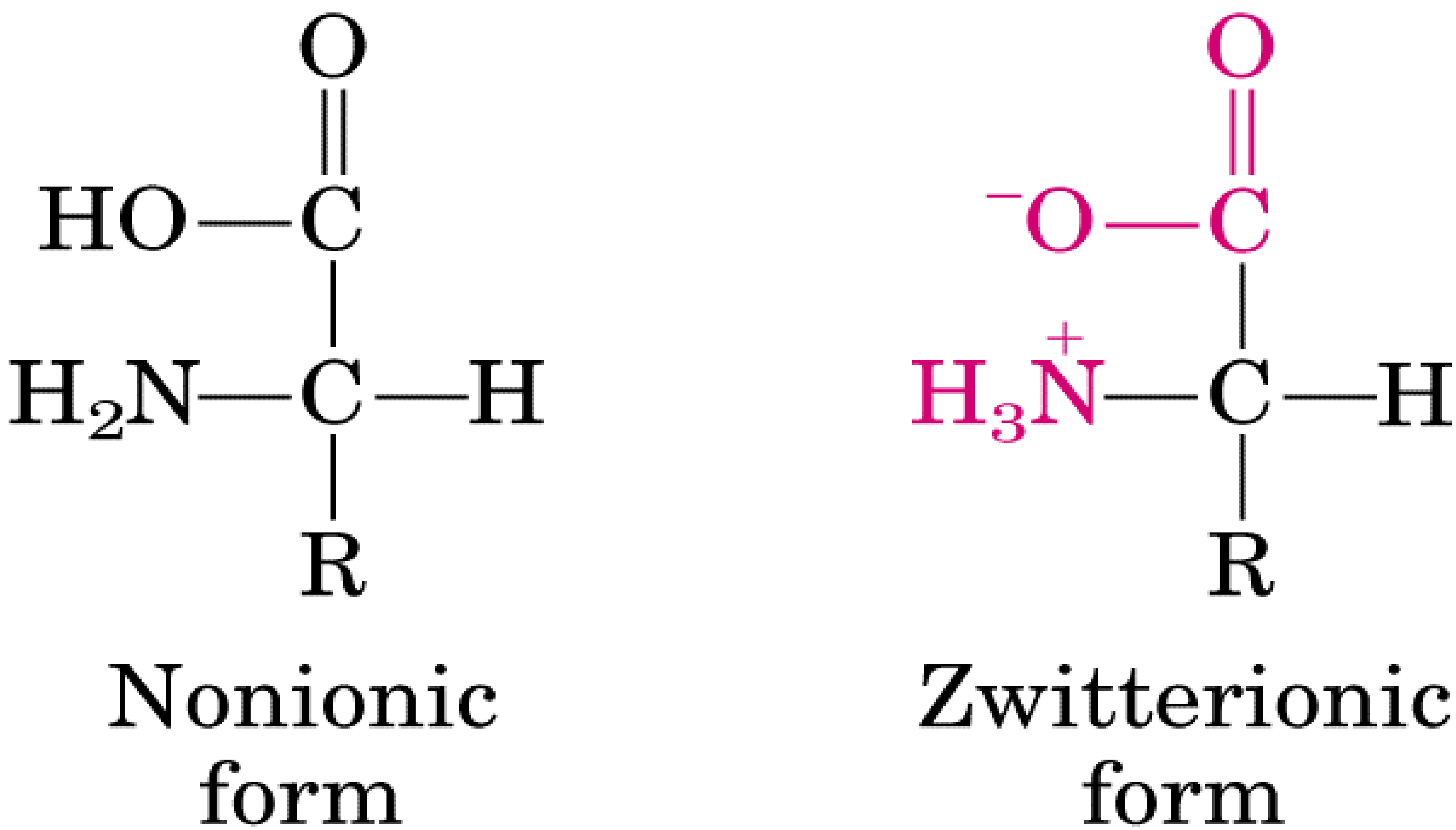
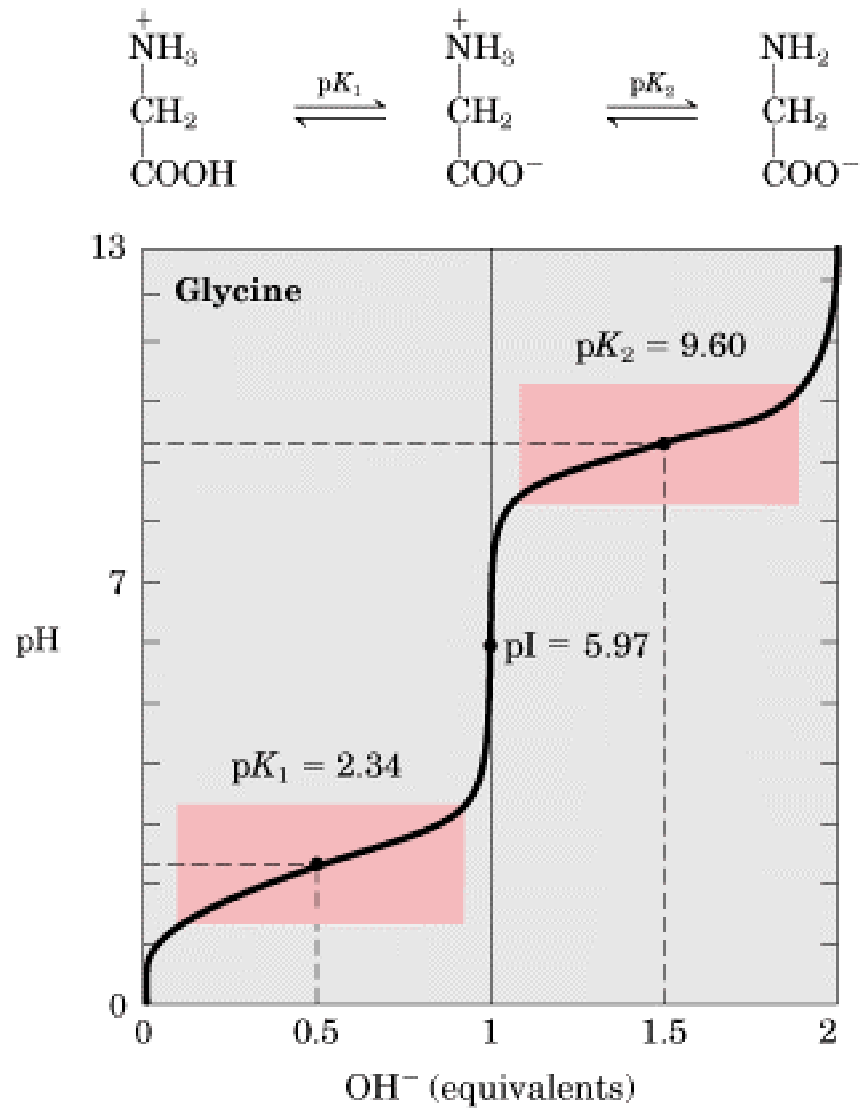
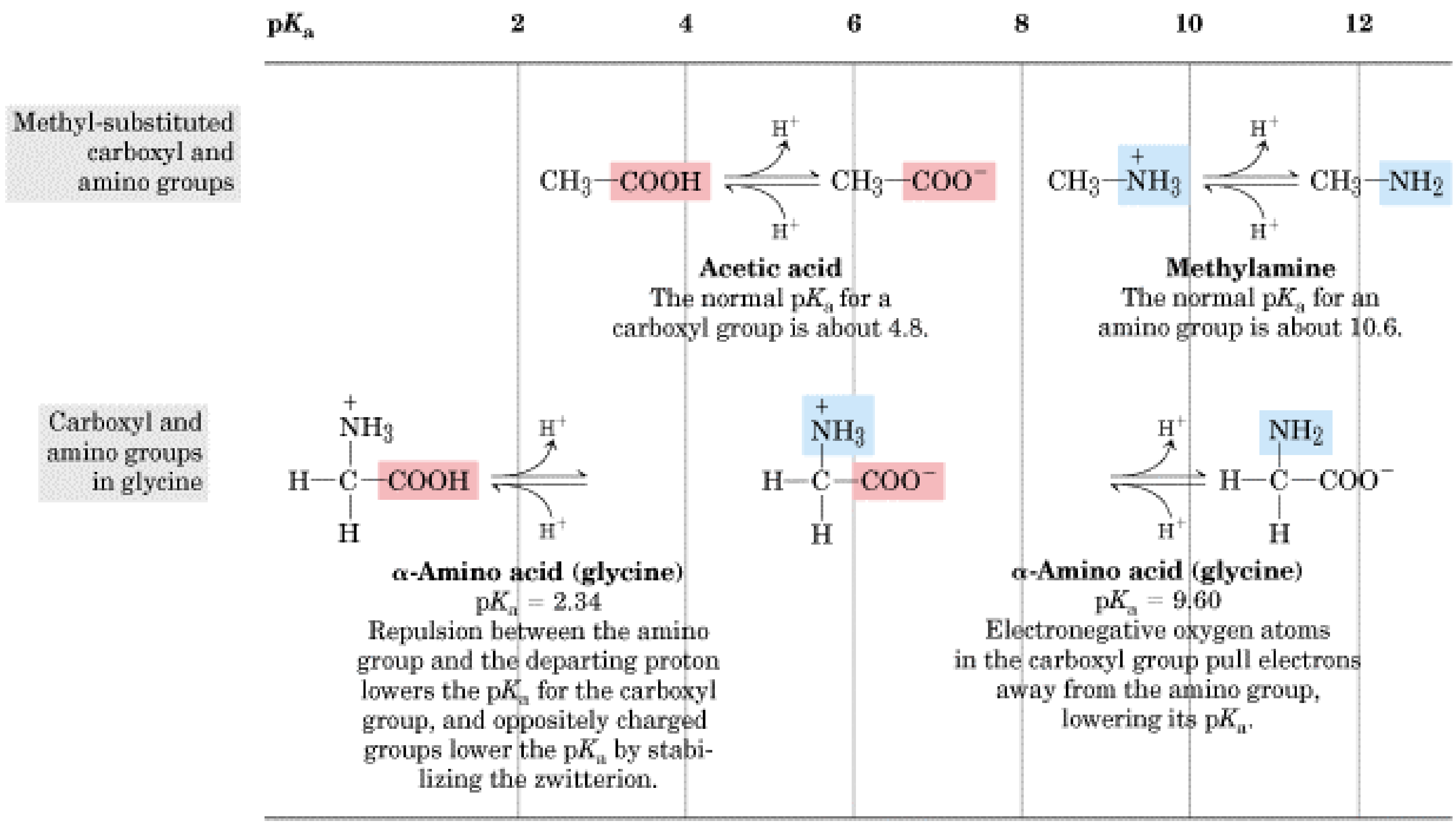


Nonionic and Zwitterionic forms of amino acids: The nonionic form does not occur in significant amounts in aqueous solutions. The zwitterion predominates at neutral pH.

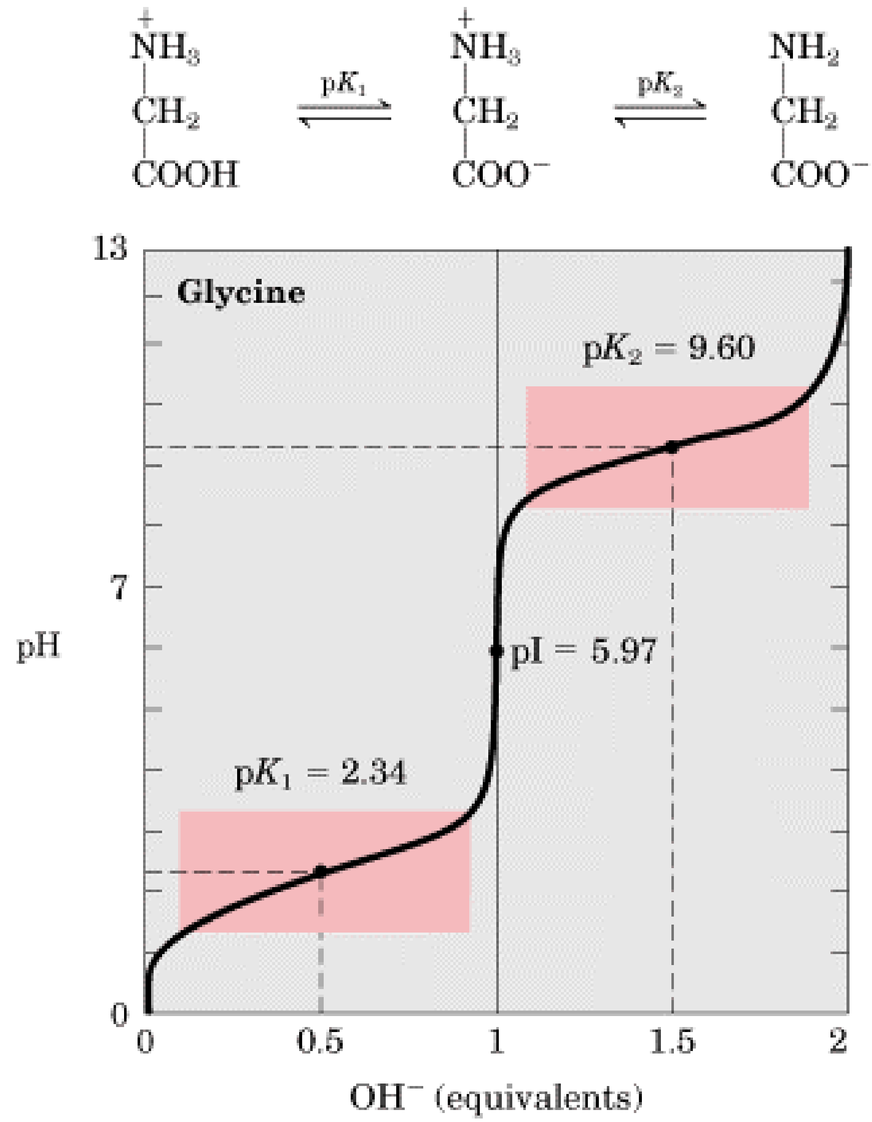
Amino Acids Have Characteristic Titration Curves: Shown here is the titration curve of 0.1M glycine (G) at 25^oC. The ionic species predominating at key points in the titration are shown above the graph. The shaded boxes, centered at about $pK_1 = 2.34$ and $pK_2 = 9.60$, indicate the regions of greatest buffering power.





. **Effect of the chemical environment on pK_a:** the pK_a values for the ionizable groups in glycine (G) are lower than those for simple, methyl-substituted amino and carboxyl groups. These downward perturbations of pK_a are due to intramolecular interactions. Similar effects can be caused by groups that happen to be positioned nearby – for example in the active site of an enzyme

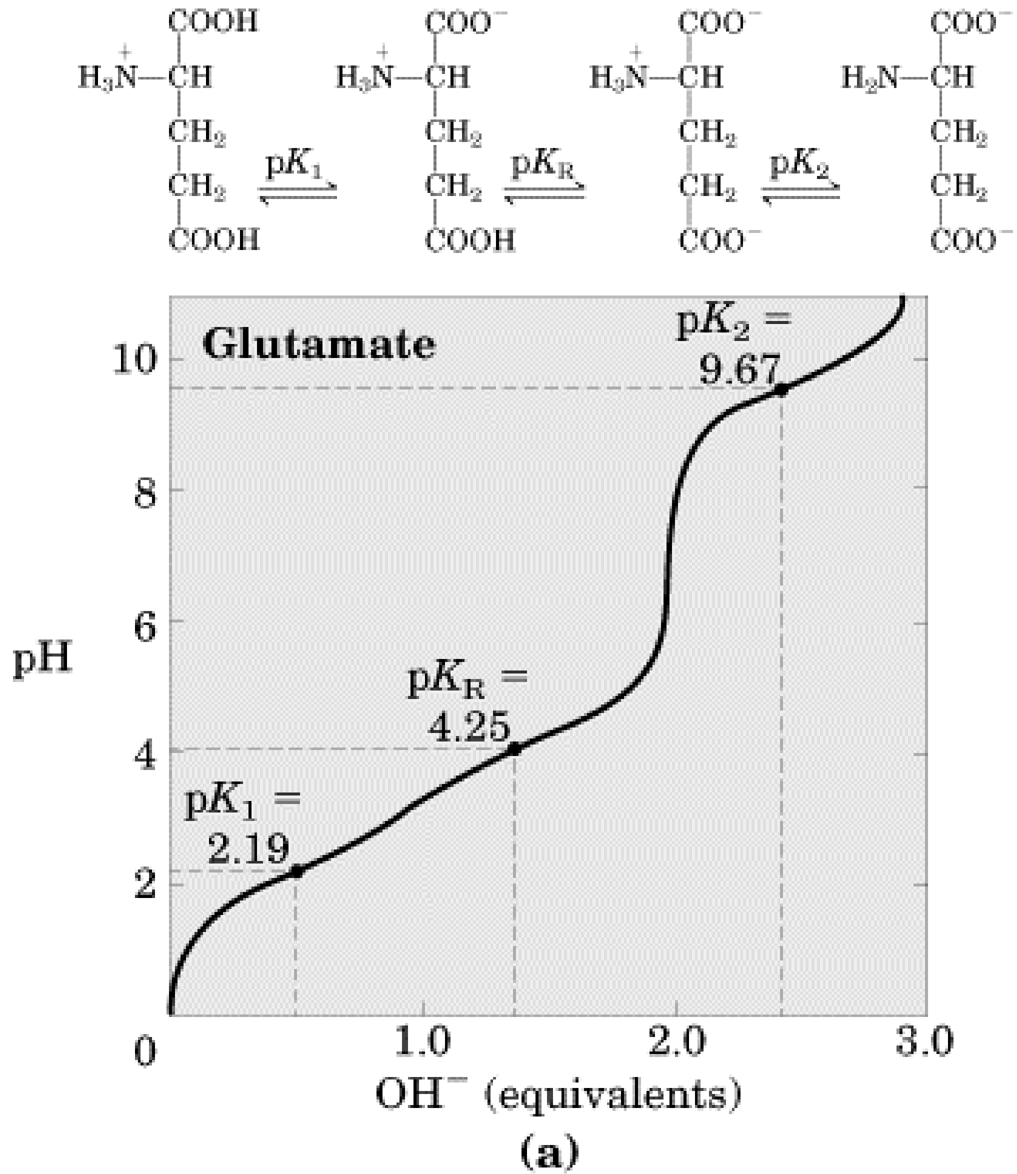
Titration Curves Predict the Electric Charge of Amino Acids: At pH 5.97, glycine is present predominantly as its dipolar form, fully ionized but with no *net* electric charge. The characteristic pH at which the net electric charge is zero is called the **isoelectric point**, designated **pI**. For glycine, which has no ionizable groups in its side chain, the isoelectric point is simply the arithmetic mean of the two pK_a values.



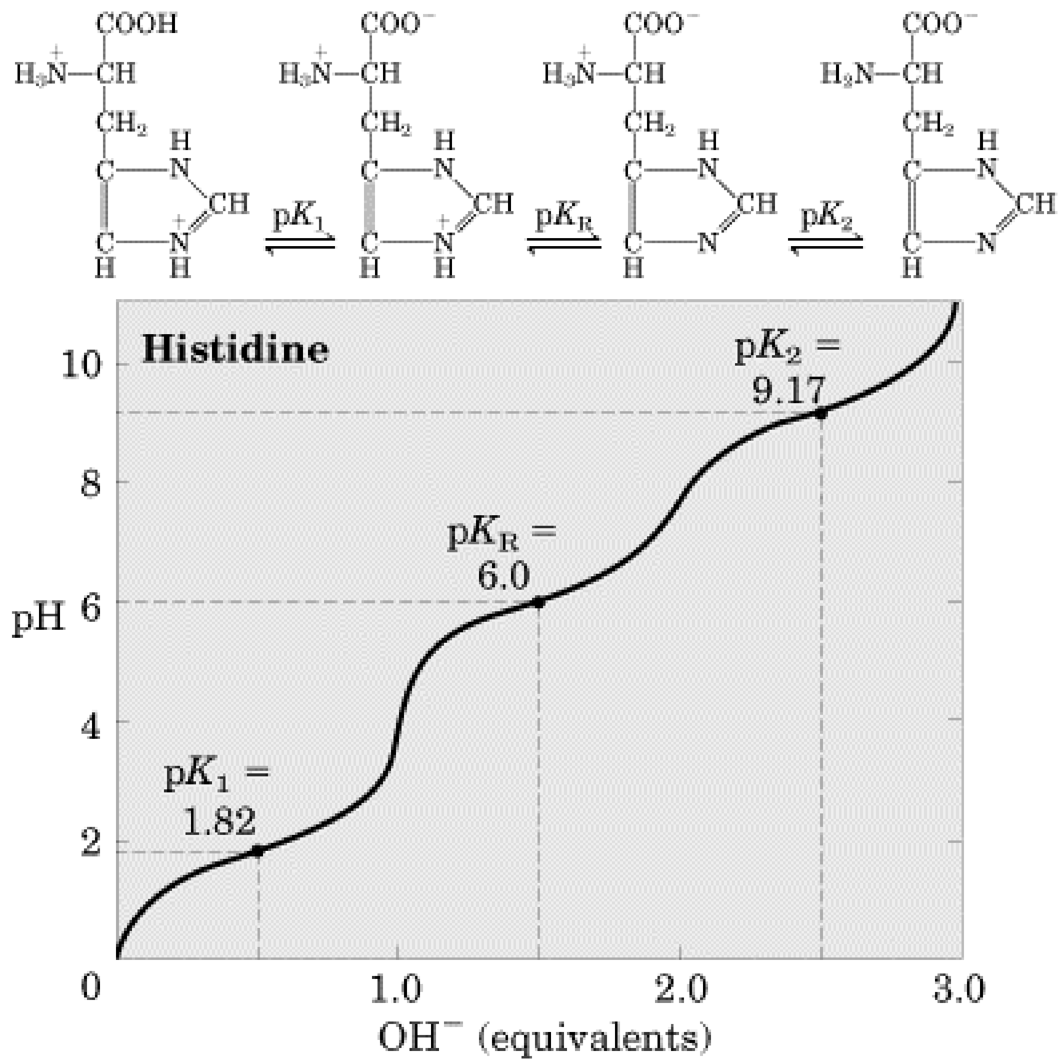
Amino Acids Differ in Their Acid-Base Properties

- Amino acids with an ionizable R group have more complex titration curves, with three stages corresponding to the three possible ionization steps; thus they have three pK_a values.
- The additional stage for the titration of the ionizable R group merges to some extent with the other two.
- The isoelectric points reflect the nature of the ionizing R groups present.

Titration Curve for Glutamate (E): Glutamate has a pI of 3.22, considerably lower than that of glycine. This is due to the presence of <u>two</u> carboxyl groups which, at the average of their pK_a values (3.22), contribute a net negative charge of –1 that balances the +1 contributed by the amino group. The pK_a of the R group is designated here as pK_R.



Titration Curve for Histidine (H): The pI of Histidine, with two groups that are positively charged when protonated, is 7.59 (the average of the pK_a values of the amino and imidazole groups). Note that Histidine has an R group (pK_R=6.0) providing significant buffering power near neutral pH. No other amino acid has an ionizable side chain with a pK_a value near enough to pH 7.0 to be an effective physiological buffer.



(b)

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